Theravance Biopharma, Inc. Announces Top-line Results from a Phase 3 Study of Ampreloxetine in Patients with Symptomatic Neurogenic Orthostatic Hypotension

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- Randomized, double-blind, placebo-controlled study did not meet the primary endpoint: improvement in OHSA #1 in patients receiving ampreloxetine for four weeks compared to placebo

DUBLIN and SOUTH SAN FRANCISCO, Calif., Sept, 15, 2021 /PRNewswire/ -- Theravance Biopharma, Inc. ("Theravance Biopharma" or the "Company") (NASDAQ: TBPH), a diversified biopharmaceutical company primarily focused on the discovery, development, and commercialization of organ-selective medicines, today announced top-line results from a Phase 3 randomized, double-blind, placebo-controlled multi-center Phase 3 study assessing the safety and efficacy of ampreloxetine compared to placebo for the treatment of symptomatic neurogenic orthostatic hypotension (nOH).

The study did not meet its primary endpoint. The majority of treatment-related adverse events were mild or moderate in severity. Serious adverse events occurred in two patients on placebo and four on ampreloxetine and none were considered related to the study drug; no deaths were reported. There was no signal for supine hypertension. The Company plans to present the results at a future scientific forum.

"These are not the results we had hoped to achieve, especially given the clear unmet need for patients suffering from symptomatic nOH and the positive top-line four-week results from the Phase 2 study announced in 2018. We will continue to analyze the data to better understand the findings," said Rick E Winningham, Chief Executive Officer, Theravance Biopharma. *"We are grateful to all those who dedicated their time and efforts to progress this study, especially during the challenges of the pandemic. We are hopeful that insights from this study may inform future drug development to help those with this debilitating condition."*

In light of these results, the Company will be determining the appropriate next steps for Study 0170 (NCT03829657; more than 75% enrolled) and Study 0171 (NCT04095793); clinical trial sites will be notified accordingly.

About the Phase 3 Study

Study 0169 (NCT03750552) was a Phase 3, 4-week, randomized, double-blind, placebo-controlled, parallel-group study to evaluate the efficacy and safety of ampreloxetine compared to placebo in patients with symptomatic nOH (n=195). Patients from Study 0169 were eligible to enter into Study 0170, a Phase 3, 22-week, multi-center, randomized withdrawal study to evaluate the sustained benefit in efficacy and safety of ampreloxetine in patients with symptomatic nOH.

About Symptomatic nOH

Neurogenic orthostatic hypotension (nOH) is a rare disorder defined as a sustained orthostatic fall in systolic blood pressure (SBP) of ≥ 20 mm Hg or diastolic blood pressure (DBP) of ≥ 10 mm Hg within three minutes of standing. Severely affected patients are unable to stand for more than a few seconds because of their decrease in blood pressure, leading to cerebral hypoperfusion and syncope. A debilitating condition, nOH results in a range of symptoms including dizziness, lightheadedness, fainting, fatigue, blurry vision, weakness, trouble concentrating, and head and neck pain. nOH is caused by autonomic nervous system malfunction and is associated with several underlying medical conditions including multiple system atrophy (MSA), pure autonomic failure (PAF), and Parkinson's disease (PD).

About OHSA #1

OHSA #1 is an endpoint that is part of the Orthostatic Hypotension Questionnaire, a validated scale assessing the presence of a range of hypotension-related symptoms including dizziness, weakness, problems with vision, fatigue, trouble concentrating, and head/neck discomfort. It is based on a scale from 0 (no symptoms) to 10 (worst possible severity of a symptom), with reductions in OHSA points indicating symptom improvement and increases in OHSA score indicating symptom worsening. OHSA #1 specifically measures patients' dizziness, lightheadedness, feeling faint, or feeling like they might black out. OHSA #1 has been accepted as a suitable endpoint in the investigation of neurogenic orthostatic hypotension by regulatory agencies.

About Ampreloxetine

Ampreloxetine (TD-9855) is an investigational, Theravance Biopharma-discovered, potent, long-acting, once-daily norepinephrine reuptake inhibitor in development for the treatment of symptomatic neurogenic orthostatic hypotension (nOH).

About Theravance Biopharma

Theravance Biopharma, Inc. is a diversified biopharmaceutical company primarily focused on the discovery, development and commercialization of organ-selective medicines. Its purpose is to pioneer a new generation of small molecule drugs designed to better meet patient needs. Its research is focused in the areas of inflammation and immunology.

In pursuit of its purpose, Theravance Biopharma applies insights and innovation at each stage of its business and utilizes its internal capabilities and those of partners around the world. The Company applies organ-selective expertise to target disease biologically, to discover and develop medicines that may expand the therapeutic index with the goal of maximizing efficacy and limiting systemic side effects. These efforts leverage years of experience in developing lung-selective medicines to treat respiratory disease, including FDA-approved YUPELRI® (revefenacin) inhalation solution indicated for the maintenance treatment of patients with chronic obstructive pulmonary disease (COPD). Its pipeline of internally discovered programs is targeted to address significant patient needs.

Theravance Biopharma has an economic interest in potential future payments from Glaxo Group Limited or one of its affiliates (GSK) pursuant to its agreements with Innoviva, Inc. relating to certain programs, including TRELEGY.

For more information, please visit www.theravance.com.

Forward-Looking Statements

This press release contains certain "forward-looking" statements as that term is defined in the Private Securities Litigation Reform Act of 1995 regarding, among other things, statements relating to goals, plans, objectives, expectations and future events. Theravance Biopharma intends such forward-looking statements to be covered by the safe harbor provisions for forward-looking statements contained in Section 21E of the Securities Exchange Act of 1934 and the Private Securities Litigation Reform Act of 1995. Examples of such statements include statements relating to: the Company's goals, designs, strategies, plans and objectives, the potential characteristics, benefits and mechanisms of action of the Company's product and product candidates, and interpretation of the results of our clinical trials or conclusions drawn therefrom. These statements are based on the current estimates and assumptions of the management of Theravance Biopharma as of the date of the press release and are subject to risks, uncertainties, changes in circumstances, assumptions and other factors that may cause the actual results of Theravance Biopharma to be materially different from those reflected in the forward-looking statements. Important factors that could cause actual results to differ materially from those indicated by such forward-looking statements include, among others, risks related to: disagreements with Innoviva, Inc. and TRC LLC, the uncertainty of arbitration and litigation and the possibility that the results of these proceedings could be adverse to the Company, and additional future analysis of the data resulting from our clinical trial(s). Other risks affecting Theravance Biopharma are in the Company's Form 10-Q filed with the SEC on August 5, 2021 and other periodic reports filed with the SEC. In addition to the risks described above and in Theravance Biopharma's filings with the SEC, other unknown or unpredictable factors also could affect Theravance Biopharma's results. No forward-looking statements can be guaranteed, and actual results may differ materially from such statements. Given these uncertainties, you should not place undue reliance on these forward-looking statements. Theravance Biopharma assumes no obligation to update its forward-looking statements on account of new information, future events or otherwise, except as required by law.

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